to characterize the underlying disease progression parameters and strengthen these assessments.

PRM90

OVERVIEW OF HEALTH ECONOMIC MODELS IN TYPE 2 DIABETES MELLITUS (T2DM); A SYSTEMATIC LITERATURE REVIEW

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OBJECTIVES: To identify and compare economic models developed to evaluate the cost-effectiveness of treatments for type 2 diabetes mellitus (T2DM), and their use in health care decision-making. **METHODS:** This research updates two previously published systematic reviews. The current systematic literature review was performed according to a pre-defined search strategy and review criteria in six commonly used databases from September 2008 to January 2013. In addition, websites of Health Technology Assessment (HTA) organizations across nine countries and major disease conferences' proceedings were also reviewed. For each identified model, key information was extracted and assessed. **RESULTS:** Overall, 2262 citations were identified; 122 full text publications, 169 conference proceedings and 106 HTA reports met the pre-defined inclusion criteria. Among these, 27 models were identified; 6 from full text publications, 18 models from conference proceedings, and 3 models from HTA reports. Most of the included models applied a similar model structure, either using Markov-modelling or micro-simulation techniques, and were based on similar key data sources. A key challenge of T2DM economic modelling is to appropriately predict the long-term progression of relevant risk factors and translate these into clinical and economical consequences of diabetes-related complications. In line with previous findings, the UKPDS risk equations were most commonly used for the above purposes in the newly identified models. Among published studies and HTA submissions, T2DM economic models that are widely published and accepted by HTAs include CARDIFF and CORE. **CONCLUSIONS:** The most commonly employed models in HTA submissions, namely CARDIFF and CORE, have similar techniques to forecast future costs and health outcomes. Hence, the focus for decision makers should be to consider the appropriateness of the critical assumptions regarding data inputs that impact the results.

PRM91

NETWORK META-ANALYSIS WITH FRACTIONAL POLYNOMIALS FOR REPEATED TROUGH FEV1 MEASURES IN COPD: ACLIDINIUM BROMIDE 400 µG BID VERSUS TIOTROPIUM 18 µG QD

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OBJECTIVES: To estimate the relative efficacy of aclidinium bromide 400 µg BID (AB400), to tiotropium bromide 18 µg QD (TIO18) by means of lung function in patients with COPD, within the first 24 weeks of treatment and illustrate the repeated measures network meta-analysis (NMA) models. **METHODS:** A systematic literature search using a predefined strategy in MEDLINE, EMBASE and the Cochrane Library identified 16 unique placebo-controlled RCTs reporting FEV_1 trough: TIO18 (n=13) and AB400 (n=3). The development of trough FEV_1over time for AB400, TIO18 and placebo (PLA) was modeled with fractional polynomials, and the difference between the parameters of these polynomials within a trial were synthesized across studies with a Bayesian NMA. This type of NMA allows for the simultaneous analysis of outcomes at multiple time points. The within-trial correlation was not available from the publications of the included studies, and as such a sensitivity analyses was performed assuming different values for the correlation. **RESULTS:** Given the fractional polynomial parameters obtained with the NMA model, the corresponding treatment effects over time for AB400 vs TIO18, AB400 vs PLA and TIO vs PLA were estimated. The model with $t^{-0.5}$and log(t) had the best fit according to the deviance information criterion (DIC). These polynomials and within study correlation were used for the modeling of the outcomes over time. AB400 is equally efficacious compared to TIO18 during the first 24 weeks, as the 95% CrI of the difference in CFB between the treatments includes zero while the mean is <15mL. Furthermore, the probability that each treatment was best was calculated as a function of time. **CONCLUSIONS:** This analysis demonstrates the use of the proposed NMA models and suggests that maintenance treatment with AB400 results in comparable improvements in lung function, as TIO18 in COPD patients over a 24 weeks period.

PRM92

EVPI CURVES IN PRACTICE

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When making decisions about the allocation of scarce health-care resources it's not only important to consider the estimated cost-effectiveness (CE) with current evidence, but also the value of additional research. Expected value of perfect information (EVPI) is the amount a decision maker should be willing to pay to eliminate uncertainty surrounding the decision about which option is optimal for different levels of the CE threshold (λ). Although EVPI analysis is being requested increasingly by reimbursement agencies there is still limited literature on the interpretation of EVPI curves. The typical 'textbook' example represents just one of the possible shapes that the curve can take. **OBJECTIVES:** To explore and explain different shapes of EVPI curves based on the position of alternative treatment choices on the incremental cost-effectiveness plane. **METHODS:** A hypothetical probabilistic decision model was developed in which two interventions were compared. Key input parameters were varied to force the model outcomes into different quadrants on the incremental CE plane. The population EVPI, based on a hypothetical number of future patients and the estimated lifetime of the new intervention, was plotted. **RESULTS AND CONCLUSIONS:** The result of this study demonstrates a number of scenarios where the EVPI curve takes a different form compared to the one illustrated in the typical 'textbook' example. For example, when the majority of the plotted outcomes are spread over the northern quadrants the traditional EVPI peak is absent, and this could be explained by the fact that the reduction in decision uncertainty does not outweigh the increased value of opportunity loss. Further, plots spread over the eastern quadrants present a maximum EVPI at zero λ which then gradually decreases. This study may inform the interpretation of EVPI curves, and add value to the analysis of the value of additional research.

PRM93

MODELING MEDICATION ADHERENCE IN COMPARATIVE EFFECTIVENESS RESEARCH

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OBJECTIVES: Real-world patients do not exhibit the level of medication adherence seen in clinical trials. Hence, the effectiveness of medications in routine practice may differ. It is important to understand the manifestations of suboptimal medication adherence in a population to assess the potential of adherence-improving interventions and the real-world value of medications. The objective of our study was to compare the clinical outcomes of an adherence naïve framework versus a dynamic adherence framework using the case of statins for primary prevention of cardiovascular disease versus no statin use. **METHODS:** Statin adherence was categorized as PDC≤.20, .20<PDC<.80 and PDC≥ .80 based on a longitudinal epidemiological cohort study of US medical and pharmacy claims. Yearly adherence transitions were incorporated into a Markov microsimulation using Treeage software. Tracker variables were used to store adherence transitions which were then used to adjust probabilities of cardiovascular events (MI, stroke, acute angina) over the patient's lifetime. Statin effectiveness was adjusted between 0% and 100% of trial-based risk reduction. A total of 10,000 microsimulations were used to estimate incremental effectiveness as CV events avoided and quality-adjusted life-years (QALYs). **RESULTS:** In the 10,000-patient statin user cohort simulated by the adherence-naïve model, it was estimated that statin use resulted in 1,162 CV events avoided and 0.39 QALYs gained over a lifetime horizon. The dynamic adherence model estimated that 42% of patients exhibited highest adherence, 40% exhibited intermediate adherence and 18% exhibited low adherence. This model simulated that overall, statin use resulted in 366 events were avoided and 0.18 QALYs gained. **CONCLUSIONS:** A Markov microsimulation used to simulate changes in patients' medication adherence over time reveals differential risk reduction and effectiveness in terms of CV events and QALYs gained. The framework presented here is useful for comparing drugs in which optimal effectiveness and costs may be similar, but differential adherence may affect outcomes.

PRM94

CAUSAL ANALYSIS OF LONGITUDINAL PATIENT TURNOVER DATA AT HEPATITIS-C

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OBJECTIVES: In recent years the financer in Hungary (NHIFA) has established a detailed and stabile patient turnover database, which reflects time dependent changes. Meanwhile, statistical methods of longitudinal data revealing causal relationship have been becoming widespread. By these new methods, analyses similar to assessment of randomized clinical trials have become available. In our research we studied the causal effects of the strategy of treatment, especially the frequency of retreatment of responder patients on features of status, events and costs of patients diagnosed Hepatitis C. **METHODS:** Causal inference on longitudinal (e.g. patient path) data is possible using the methods of Robins (1999). It makes therapy history exogenous, i.e. independent of the actual status of the patient via dynamical, time dependent reweighting of individual patient paths. Consequently, patient paths can be analyzed similarly to cohort data assessment of randomized clinical trials. The method can be used to confirm the results of RCTs. It can substitute RCTs, too, e.g. if RCTs are ethically impossible. **RESULTS:** We obtained by applying Robins' method that repeated combination therapies decreased the risk of liver related complications and the development of hepatocellular carcinoma. The method applied to cost analysis revealed that despite repeated therapies the costs of newly developed cirrhosis and tumor are higher than the corresponding costs of patients with sustained viral response. **CONCLUSIONS:** Robins'method is appropriate for measuring the causal effects of certain factors of care on patient pathways, especially if patient turnover data are supplemented with physiologic, diagnostic and lab information found in clinical registers.

PRM95

APPROPRIATE EVIDENCE SOURCES FOR POPULATING DECISION ANALYTIC MODELS WITHIN HEALTH TECHNOLOGY ASSESSMENT (HTA): A SYSTEMATIC REVIEW OF HTA MANUALS AND HEALTH ECONOMIC GUIDELINES

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OBJECTIVES: Decision analytic modellers use numerous types of evidence for populating model parameters. Detailed methodological advice on which type of data is to be used for what type of model parameter is required. We aim at reviewing existing HTA manuals and health economic (modelling) guidelines in order to gain advice on appropriate evidence sources for populating models. **METHODS:** We identified manuals and guidelines via the International Network of Agencies for Health Technology Assessment (INAHTA) and by hand search. We included documents from Europe, the USA, Canada, Australia and New Zealand as well as transnational guidelines written in English or German. We systematically sum-